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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,924	05/04/2001	Fred E. Regnier	290.0001 0101	8955

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EXAMINER
TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
1639	17

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/849,924	Applicant(s) REGNIER ET AL.	
	Examiner My-Chau T. Tran	Art Unit 1639	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment filed 3/24/03 in Paper No. 14 is acknowledged and entered. Claims 33-99 are canceled by the amendment.

Information Disclosure Statement

2. The information disclosure statement filed 3/24/03 in Paper No. 16 is acknowledged and considered by the examiner. It is noted the copies maybe lost in the mail.

Inventorship

3. In view of the papers filed 3/24/03, the inventorship in this nonprovisional application has been changed by the deletion of Xiang Zhang and Asish Chakraborty as named inventor.

PP 6/16/03

The inventorship is acknowledged and corrected.

4. Claims 1-32 are pending.

Withdrawn Rejections

5. The previous rejections 35 USC 112, second/first paragraph, for claims 1-32 have been withdrawn in view of applicant's argument.

6. The previous rejections under 35 USC 102(a) as being anticipated by Chen et al. (*Anal. Chem.*, **2000**, 72(6):1134-1143) for claims 1-4 and 6 have been withdrawn in view of applicant's amendments of claims argument.

7. The declaration under 37 CFR 1.132 filed 3/24/03 is sufficient to overcome the rejection of claims 1-32 based upon the two co-authors, Minghui Geng and Junyan Ji, of Geng et al. (*Journal of Chromatography A*, **2000**, 870(1-2):295-313).

8. Upon further consideration, the following new grounds of rejection are made as follows. Therefore, this Office action is a non-final rejection.

9. Claims 1-32 are treated on the merit in this Office Action.

New Rejections

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1-4, 6-13, 17-21, and 23-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Gygi et al. (*Nature Biotechnology*, **1999**, 17(10):994-999).

Gygi et al. disclosed a method for quantitative analysis of complex protein mixtures using isotope-coded affinity tags (ICAT) (Abstract; pg. 994, right col., 6-9). The method comprises of the following steps: 1) The side chains of cysteinyl residues in a reduced protein sample representing one cell state are derivatized with the isotopically light form of the ICAT reagent. The equivalent groups in a sample representing a second cell state are derivatized with the isotopically heavy reagent. (2) The two samples are combined and enzymatically cleaved to generate peptide fragments (refers to the fragmenting step). (3) The tagged (cysteine-containing) peptides (refers to the attaching step) are isolated by avidin affinity chromatography (refers to the fractionating step). (4) Finally, the isolated peptides are separated and analyzed by LC-MS/MS (electrospray ionization (ESI) MS/MS, in conjunction with microcapillary liquid chromatography (LC)) (pg. 994, right col., 12-24; figure 2). Therefore, the method of Gygi et al. anticipates the presently claimed invention.

12. Claims 1-4, 6-13, 17-21, and 23-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Chait et al. (US Patent 6,391,649 B1).

Chait et al. disclosed a method for accurately comparing the levels of cellular components, such as proteins, present in samples, which differ in some respect from each other

using mass spectroscopy and isotopic labeling (Abstract). The method comprises of the following steps: 1) Two cell pools are prepared. One of the cell pools, here Cell Pool 1, contains a cell culture grown or maintained in a medium containing a natural abundance of isotopes. The other cell pool contains a cell culture grown or maintained in a medium in which one or more isotopes of nitrogen, carbon, oxygen or sulfur, for example, is not present in a natural abundance. 2) All or portions of the cell pools are then combined. 3) The proteins are extracted from the combined cell pool in a manner known in the art such as digestion. 4) The mixture of proteins is then separated into the individual proteins or small groups of proteins, also by known techniques, such as affinity binding. 5) The separated proteins are then preferably digested into peptides. 6) The proteins or digested proteins are then subjected to mass spectroscopy. Any mass spectrometer may be used to analyze the peptides or proteins. For example, the mass spectrometer may be a Matrix-Assisted Laser Desorption/Ionization ("MALDI") Time-of-Flight ("TOF") Mass Spectrometer, an Electrospray Ionization ("ESI") ion trap mass spectrometer, or an ESI quadrupole mass spectrometer. Therefore, the method of Chait et al. anticipates the presently claimed invention.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 5, 14-16, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gygi et al. (*Nature Biotechnology*, **1999**, 17(10):994-999).

Gygi et al. disclosed a method for quantitative analysis of complex protein mixtures using isotope-coded affinity tags (ICAT) (Abstract; pg. 994, right col., 6-9). The method comprises of the following steps: 1) The side chains of cysteinyl residues in a reduced protein sample representing one cell state are derivatized with the isotopically light form of the ICAT reagent. The equivalent groups in a sample representing a second cell state are derivatized with the isotopically heavy reagent. (2) The two samples are combined and enzymatically cleaved to generate peptide fragments (refers to the fragmenting step). (3) The tagged (cysteine-containing) peptides (refers to the attaching step) are isolated by avidin affinity chromatography (refers to the fractionating step). (4) Finally, the isolated peptides are separated and analyzed by LC-MS/MS (electrospray ionization (ESI) MS/MS, in conjunction with microcapillary liquid chromatography (LC)) (pg. 994, right col., 12-24; figure 2). Therefore, the method of Gygi et al. anticipates the presently claimed invention.

The method of Gygi et al. does not expressly disclose that the fragmenting step occurs before the isotopic labeling step.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the fragmenting step occurs before the isotopic labeling step in the method of Gygi et al. One of ordinary skill in the art would have been motivated to include the fragmenting step occurs before the isotopic labeling step in the method of Gygi et al. because the order in which the fragmenting step occurs would be a choice as experimental design and is considered within the purview of the prior art.

15. Claims 5, 14-16, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chait et al. (US Patent 6,391,649 B1).

Chait et al. disclosed a method for accurately comparing the levels of cellular components, such as proteins, present in samples, which differ in some respect from each other using mass spectroscopy and isotopic labeling (Abstract). The method comprises of the following steps: 1) Two cell pools are prepared. One of the cell pools, here Cell Pool 1, contains a cell culture grown or maintained in a medium containing a natural abundance of isotopes. The other cell pool contains a cell culture grown or maintained in a medium in which one or more isotopes of nitrogen, carbon, oxygen or sulfur, for example, is not present in a natural abundance. 2) All or portions of the cell pools are then combined. 3) The proteins are extracted from the combined cell pool in a manner known in the art such as digestion. 4) The mixture of proteins is then separated into the individual proteins or small groups of proteins, also by known techniques, such as affinity binding. 5) The separated proteins are then preferably digested into peptides. 6) The proteins or digested proteins are then subjected to mass spectroscopy. Any mass spectrometer may be used to analyze the peptides or proteins. For example, the mass spectrometer may be a Matrix-Assisted Laser Desorption/Ionization ("MALDI") Time-of-Flight ("TOF") Mass Spectrometer, an Electrospray Ionization ("ESI") ion trap mass spectrometer, or an ESI quadrupole mass spectrometer.

The method of Chait et al. does not expressly disclose that the fragmenting step occurs before the isotopic labeling step.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the fragmenting step occurs before the isotopic labeling step in

the method of Chait et al. One of ordinary skill in the art would have been motivated to include the fragmenting step occurs before the isotopic labeling step in the method of Chait et al. because the order in which the fragmenting step occurs would be a choice as experimental design and is considered within the purview of the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct
June 13, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER